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| APPLICATION NO.  | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.       | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------------|------------------|
| 09/981,312   | 10/15/2001  | Mitchell A. Avery    | 1786                      | 4970             |
| 29003  | 7590        | 06/25/2004           |                           |                  |
| TIMOTHY J. MARTIN, P.C.<br>9250 W. 5TH AVENUE, SUITE 200<br>LAKEWOOD, CO 80226 |             |                      | EXAMINER<br>POWERS, FIONA |                  |
|  |             |                      | ART UNIT                  | PAPER NUMBER     |
|  |             |                      | 1626                      |                  |

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/981,312

Applicant(s)

AVERY, MITCHELL A.

Examiner

Fiona T. Powers

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 23 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-34,69-72 and 74-78 is/are pending in the application.
- 4a) Of the above claim(s) 75-78 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-7,9,15-17,33,34,69-72 and 74 is/are rejected.
- 7) ☒ Claim(s) 3,8,10-14 and 18-32 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 4/23/04, 4/28/04.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

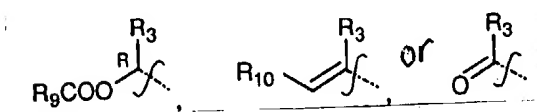
Art Unit: 1626

Receipt is acknowledged of the information disclosure statements filed April 23, 2004 and April 28, 2004 and the amendment filed April 23, 2004, which have been entered in the file.

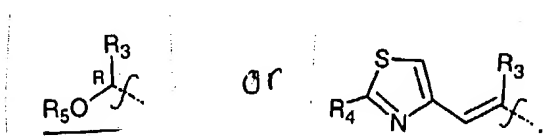
Applicant's election with traverse of the species wherein A is  $\text{CHR}^3\text{-OR}^5$  in the reply filed on March 29, 2004 is acknowledged. The traversal is on the ground(s) that the number of species in the application is reasonable and a consolidated examination would not be burdensome. This is found persuasive. The requirement is hereby withdrawn.

Claims 13 and 34 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 34 is not a further limitation of claim 33 when W is



because in claim 33 the compound formed is the fourth compound of claim 1 wherein A which corresponds to W can only be



Art Unit: 1626

Claim 13 is not a further limitation of claim 12 because for the sixth compound, the radical represented by D in claim 13 is different from the radical D in claim 12.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34 and 69 to 71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Variables  $R_1$ ,  $R_9$  and  $R_{10}$  are defined in claim 34 but they do not appear in the formula.

Variables  $R_6$ ,  $R_{11}$  and  $R_{12}$  are defined in claims 69 and 70 but do not appear in the formula.

Claims 71 and 72 define the variables x and y which appear in the radicals defined for  $R_{11}$  and  $R_{12}$  in claim 70, but  $R_{11}$  and  $R_{12}$  do not appear in the formula.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Art Unit: 1626

Claims 1, 2, 4 to 7, 9, 15 to 17, 33, 34, 69 to 72 and 74 are rejected under 35 U.S.C. 102(b) as being anticipated by Nicolaou et al. (J. Am. Chem. Soc., 119(34), 7974-7991, 1997), cited by applicant.

The reference discloses the claimed process which comprises an aldol condensation of a first compound wherein  $R^1$ ,  $R^2$ ,  $R^3$  and  $R^4$  are methyl and  $R^6$  is the protecting group TBS and Z is the thiazole radical, with a second compound  $R_{13}OOCCH_2CHOR_7CH(CH_3)_2COCH_2CH_3$  wherein  $R_{13}$  is H and  $R_7$  is the protecting group TBS to form a third compound wherein  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$  are methyl, Z is the thiazole radical,  $R_7$  is TBS and  $R_6$  and  $R_8$  are hydrogen or the protecting group TBS, then performing macrolactonization of the third compound to form a fourth compound of the formula shown in claim 1 where A is the thiazole radical and  $R_1$ - $R_4$  are methyl and  $R_7$  and  $R_8$  are TBS or H. The fourth compound is then further converted to Epothilone B. The reference also discloses chemical compound formed by the process which is the fourth compound wherein A is the thiazole radical and  $R_1$ - $R_4$  are methyl and  $R_7$  and  $R_8$  are TBS or H or the compound of claims 34, 69 to 72 and 74 where W is the thiazole radical and  $R_2$  to  $R_4$  are methyl and  $R_7$  and  $R_8$  are H or a protecting group. Note Scheme 9 on page 7979.

Art Unit: 1626

Claims 33, 34, 69 to 72 and 74 are rejected under 35 U.S.C. 102(b) as being anticipated by Nicolaou et al. (Angew. Chem. Int. Ed., 37, 2014-2045, 1998), cited by applicant.

The reference discloses the claimed compounds wherein  $R_1$  is methyl,  $R_2$  is H or methyl,  $R_7$  and  $R_8$  are H, W (or A) is the thiazole radical wherein  $R_3$  is methyl and  $R_4$  is H, methyl, substituted alkyl or heterocyclo or W is  $R_{10}CH=CHR_3$  where  $R_3$  is methyl and  $R_{10}$  is heterocyclo or aryl. Note Compound Nos. 320, 76, 321-324, 326 and 328-334 on page 2035, Compound Nos. 375 and 377 on page 2036 and Compound No. 379 on page 2038. The compounds of instant claims 33 and 34 are the same as the compounds taught by the reference where A is the thiazole radical.

Claims 3, 8, 10 to 14 and 18 to 32 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

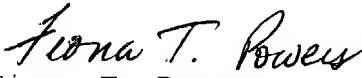
The references made of record and not relied upon show the state of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fiona T. Powers whose telephone number is (571)272-0702. The examiner can normally be reached on Monday - Friday 8:00 AM to 4:30 PM.

Art Unit: 1626

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Fiona T. Powers  
Primary Examiner  
Art Unit 1626

ftp  
June 22, 2004